

Remarks

Claims 1-5 and 8-11 are currently pending.

Double Patenting

Applicants herewith submit a terminal disclaimer with respect to U.S. Patent no. 6,241,989.

Rejection under 35 USC 103(a)

The Examiner has rejected claims 1-5 and 8-11 as being unpatentable over Esposito et al., (U.S. Patent No. 5,266,313), or Lodmel, et al. (*Journal of Virology* (1991) Volume 65, pages 3400-3405), in view of Parrish et al., (*Virology* (1988) Volume 166; pages 293-307; “Parish ’88” hereafter) or Parrish (*Virology* (1991) Volume 183; pages 195-205; “Parish ’91” hereafter); or Martyn et al., (*Journal of General Virology* (1990) Volume 71 pages 2747-53), or Carlson et al., *Journal of Virology* (1985) Volume 55; pages 574-582.

The Examiner asserts that the present claims are directed to a multivalent recombinant raccoon poxvirus that has more than one feline pathogen antigen inserted into the thymidine kinase (“TK” hereafter) site of the raccoon poxvirus, that this poxvirus can infect and replicate in feline cells, and that each of the feline antigens is expressed from a separate promoter.

In response, Applicants point out the present application makes it clear in several instances that linking each inserted gene to a separate promoter may be preferable, but is not required. See, for example, claim 1, the definition of “expression cassette” on page 8, lines 11-20, and the passage on page 11, lines 13-16. Applicants therefore request clarification of the Examiner’s position on the asserted requirement for separate promoters.

In rejecting claims 1-5 and 8-11 as unpatentable over the primary reference of Espositio et al. in view of Parrish ’88, Parrish ’91, Martyn et al. or Carlson et al. (collectively, “the secondary references” hereafter), the Examiner asserts that Esposito

et al. discloses raccoon poxviruses comprising exogenous rabies glycoprotein G gene sequences inserted within the TK site of the raccoon poxvirus, and the use of this virus in inducing protective immune responses. The Examiner argues that the secondary references disclose the cloning and nucleotide sequence of FPV V2. Based on this, the Examiner makes the conclusory statement that:

“One of ordinary skill in the art at the time the invention was made would have been motivated to express FPV V2 of Parrish et al. ('88, '91), Martyn et al. or Carlson et al. in the recombinant raccoon poxvirus of Esposito et al. to immunize against different viral pathogens.” (Office Action, pages 3-4).

In response, Applicants submit that a *prima facie* case of obviousness has not been set forth because there is no motivation to combine the cited references as the Examiner has done. Specifically, the Examiner has conceded that Esposito et al. does not teach multivalent raccoon poxviruses. However, this observation highlights the significance of the presently claimed multivalent raccoon poxviruses. In this regard, the secondary references refer only to the characterization and comparison of FPV and canine parvovirus (CPV) genomes. Therefore, one skilled in the art at the time the application was filed would not conceive of a multivalent vaccine as presently claimed based on the disclosure of a monovalent raccoon poxvirus vaccine expressing rabies G protein, and the disclosure of but one additional antigen from a feline pathogen. Thus, none of the cited references alone or in combination teach, motivate or even suggest the present invention. Applicants point out that identification of a specific motivation to combine the references is required by *In re Lee* for maintaining an obviousness rejection (277 F.3d 1338, 1343-44 (Fed. Cir. 2002). Therefore, the Examiner is respectfully requested to remove the stated rejection.

In response to the Examiner's assertion that one of ordinary skill in the art would have had a reasonable expectation of success in obtaining the present invention based upon Esposito et al. in combination with the secondary references, Applicants point out that, because there is no motivation to combine the references, it is illogical that such an expectation could be formed. However, even assuming *arguendo* that one

skilled in the art might be inclined to try combining the references as the Examiner has done, the references do not provide a reasonable expectation of success in obtaining the present invention.

Specifically, the Examiner has assumed that one would have a reasonable expectation of success because Esposito et al. disclose that the TK site of raccoon poxvirus is non-essential for viral function and encompasses a relatively large space of the poxvirus genome relative to the sizes of the rabies G and FPV V2 genes. However, the present application directly refutes this assumption where it is stated:

“Raccoon poxvirus (RCNV) was found to be safe and suitable as a viral monovalent vaccine vector useful for immunizing cats However, it was not known at the time of the invention whether raccoon poxvirus could tolerate large foreign insertions, as required when recombining multiple genes/ expression cassettes (versus a single gene), into the thymidine kinase gene ... of the raccoon poxvirus genome without the virus losing its ability to infect and replicate in susceptible host cells... Extrapolating the results of studies with VV [vaccinia virus] vectors, relative to the capacity of the viral genome to tolerate insertions... to RCNV would be presumptuous because the DNA sequences between RCNV and VV are significantly different.”
(Page 15, lines 1-19.)

Thus, it is acknowledged in the present application that raccoon poxvirus was previously known to be suitable for use as a monovalent vaccine. However, absent the teaching of the present application, there is no evidence that one skilled in the art would have a reasonable expectation of success in preparing a recombinant raccoon poxvirus as presently claimed. In furtherance of this, Applicants have submitted herewith a declaration elaborating the non-obviousness of the present invention from Dr. Joseph Esposito, the Senior Advisor on Poxvirus Infections at the Centers for Disease Control in Atlanta, Georgia, and the former Chief, Poxvirus Section of the Centers for Disease Control, and the former Director of the World Health Organization Collaborating Center for Smallpox and Other Poxvirus Infections. As described in Dr. Esposito's declaration, one skilled in the art at the time of the invention would not have conceived of the present invention. Further, even assuming

that such a conception could be formed, one would not have an expectation of success because of the technical complexity and unpredictability in making the recombinant monovalent virus vaccines known at the time.

The Examiner has also rejected claims 1-5 and 8-11 as unpatentable over Lodmell et al. in view of the secondary references. The Examiner asserts Lodmell et al. discloses raccoon poxviruses comprising exogenous rabies glycoprotein G gene sequences inserted within the TK site of the raccoon poxvirus, the use of this virus in inducing protective immune responses, and that the secondary references disclose the nucleotide and amino acid sequences of FPV V2. The Examiner concedes that Lodmell et al. (like Epsosito et al.) does not teach a recombinant poxvirus expressing more than one antigen, but also argues that one of ordinary skill would have been motivated to express FPV V2 in the recombinant raccoon poxvirus of Lodmell et al.

In response, Applicants again submit that a *prima facie* case of obviousness has not been set forth because there is no motivation to combine the cited references as the Examiner has done. The Examiner's observation that Lodmell et al. does not teach multivalent raccoon poxviruses again highlights the significance of the present invention. The secondary references refer only to the characterization and/or comparison of the FPV and CPV genomes. Therefore, one skilled in the art at the time the application was filed would not conceive of a multivalent vaccine as presently claimed based on the disclosure of a monovalent raccoon poxvirus vaccine expressing rabies G protein, and the mere disclosure of one additional antigen from a feline pathogen. None of the cited references alone or in combination teach, motivate or even suggest the present invention. Applicants again point out that identification of a specific motivation to combine the references is required by In re Lee for maintaining an obviousness rejection (277 F.3d 1338, 1343-44 (Fed. Cir. 2002). Therefore, the Examiner is respectfully requested to remove the stated rejection.

In response to the Examiner's assertion that one of ordinary skill in the art at the time of the invention would have had a reasonable expectation of success in obtaining the present invention based upon Lodmell et al. and the secondary

references, Applicants again point out that, because there is no motivation to combine the references, it is illogical that such an expectation could be formed. However, assuming *arguendo* that one skilled in the art might be inclined to try combining the references as the Examiner has done, the references do not provide a reasonable expectation of success in obtaining the present invention.

Specifically, the Examiner has made the assumption that one would have a reasonable expectation of success because Lodmell et al. discloses that the TK site of raccoon poxvirus is non-essential for viral function and encompasses a relatively large space of the poxvirus genome relative to the sizes of the rabies G and FPV V2 genes. However, the present application directly refutes this assumption on page 15, lines 1-19 (quoted above) where it is acknowledged that raccoon poxvirus was previously known to be suitable for use as a monovalent vaccine, but it was not known whether the TK site could tolerate multiple insertions without losing its replicative and infective properties. Thus, absent the teaching of the present application, there is no evidence that one skilled in the art would have a reasonable expectation of success in preparing a recombinant raccoon poxvirus as presently claimed.

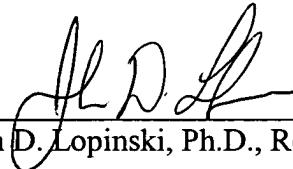
Further, in addition to acknowledging that Lodmell et al. does not disclose a recombinant virus comprising more than one foreign antigen, the Examiner has also conceded that none of the cited references teach expressing multiple exogenous genes from separate promoters. Applicants again point out that the present claims do not require independent promoters, but also that the lack of such disclosure is consistent with the observation that none of the references disclose or even suggest the recombinant raccoon poxviruses as presently claimed.

As further evidence of the non-obviousness of the present invention, and as indicated above, Applicants have appended a declaration from Dr. Joseph Esposito elaborating on the reasons the present invention is not obvious from the cited references. Accordingly, Applicants respectfully request the Examiner to remove the stated rejections and to allow all the pending claims.

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Applicants herewith request a two-month extension of time to file this response. A check for \$450.00 is enclosed. If any additional fee is due, please charge to Deposit Account No. 08-2442.

Respectfully submitted,
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